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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,306	03/23/2001	Wen Y. Chen	035879/0120	4654

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/815,306	CHEN ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *11-21,23,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,10,22,24,25 and 28-44* is/are rejected.

7)☐ Claim(s) *7-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/18/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Chen WY *et al*
Priority Date: 23 March 2000

1. The amendment filed 11/14/2002 is acknowledged and entered into the record. Accordingly, claims 28-44 are newly added. Claims 1-44 are pending, claims 11-21,23, and 26-27 were withdrawn from further consideration as being drawn to a non-elected invention.

2. Claims 1-10, 22, and 24-25, 28-44 are examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The Information Disclosure Statement filed 11/18/2002 is acknowledged and considered. A signed copy of the IDS is attached hereto.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION. Claim 25 adds the limitation of "to which the apoptosis-promoting domain binds", which is not supported in the specification or in the claims as originally filed. The new limitation further limits that the apoptosis-promoting domain inhibits by binding to STAT3 of which

is neither contemplated or suggested in the specification as filed. Applicant is required to remove such claim limitation or specifically point to support in the specification as originally filed.

Claim Rejections - 35 USC § 112 2nd paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 8 recites the limitation "prolactin domain" in line 4. There is insufficient antecedent basis for this limitation in claim 2. Claim 2 recites a prolactin-antagonzing domain but fails to recite or mention a prolactin domain in general.

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 1, 22-25, and 28-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth a protein comprising 1) a prolactin-antaonizing domain of SEQ ID No: 1; and 2) a immunomodulatory domain that is a cytokine (such as IL-2, IL-12, and IFNγ). In addition, the written description in this case has also set a fusion protein of hPRLA-IL2. However, the written description in this case is not commensurate in scope to claims that read on a protein comprising any receptor-antagonzing domain or any

apoptosis-promoting domain and any positive immunomodulatory domain as set forth in the claims.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

The following *written description* rejection is set forth herein. The claims recite a "receptor antagonizing domain", an "apoptosis-promoting domain", and a "positive immunomodulatory domain" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural features that provide the recited functions of antagonizing receptor domain, promoting apoptosis, or modulating an immune function. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient

to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice a representative number of proteins that have receptor antagonizing domains, apoptosis-promoting domains, or positive immunomodulatory domains. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the desired antagonistic, promoting or modulatory functions. The terms "receptor antagonizing domain", "apoptosis-promoting domains", and "immunomodulaory domains" can be found in many different molecules and therefore encompasses many molecules provided that they have such activities of antagonizing, promoting, or modulating. Thus the genus of compounds encompassed by these terms are extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Regarding claims that read on "truncated prolactin sequence", with the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for truncated prolactin sequences is provided in the specification on page 15 paragraph [0046] where it is disclosed that "Truncations may be made from the N- or C-terminus, but generally do not entail deleting more than aboul 30% of the native molecule. More preferably, less than about 20%, and most preferably, less than about 10%, of the native molecule is deleted. However, no disclosure, beyond the mere mention of truncations is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. No core structure or relavent characteristics that describe which portions are encompassed within the truncation is provided other than a percentage of the desired deleted amount. This is insufficient to support the broad claim of truncated prolactin sequence.

While it is noted that the instant claims are drawn to methods, the claims nevertheless require an adequate written description of the "receptor-antagonizing domain", the "apoptosis-promoting domain", and "immunomodulator domain" employed in the methods.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 102

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Larsen *et al* (WO 98/08949). Larsen *et al* teach a method of treating "metastatic conditions" with a fusion protein comprising P-selectin antagonizing fragments fused to a cytokine (see pages 6, 7,14, and 21, for example). Because the specification does not specifically exclude the types of "receptor-antagonizing domain" and defines it as any ligand that "binds to and antagonizes its cognate receptor" the fragments taught by Larsen *et al* anticipates the instantly claimed invention.

10. Claims 1,3-4, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Fell *et al* (US Patent 5,314,995). Fell *et al* teach a method of treating cancers comprising the administration of an antibody-IL-2 or antibody- IFNγ fusion protein that is specific for tumor associated markers (see col. 7 and 8). Because the specification of the instant invention defines "receptor-antagonizing domain" as "a ligand that specifically binds to a receptor "(see page 9), for the purposes of this rejection, an antibody will be defined as "a ligand that specifically binds to a receptor."

11. Claims 1,2, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Sissom *et al* (Am J. Pathol. 1988;133(3):589-95). Sissom *et al* teach a method of in vivo breast cancer treatment comprising the administration of a prolactin receptor antibody. The antibody administered to the subject was able to inhibit cancer and therefore in the absence of factual evidence to the contrary, the antibody is considered a prolactin antagonist domain. Because the specification of the instant invention defines "receptor-antagonizing domain" as "a ligand that specifically binds to a receptor

"(see page 9), for the purposes of this rejection, an antibody will be defined as "a ligand that specifically binds to a receptor." Furthermore, because the specification defines a "positive immunomodulator domain" as a domain that supports a tumor-directed positive immune response (se page 9), for the purpose of this rejection, the antibody taught by Sissom *et al* anticipates the claimed invention because the antibody inherently has the ability to reduce the amount of tumor burden in vivo by eliciting an immune response.

12. Claims 1,3, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Gillies *et al* (J. Immunology. 1998;160(12):6195-6203). Gillies *et al* teach a method of treating prostate and colon cancer comprising the administration of an antibody-IL-12 fusion protein to a subject (see abstract). Because the specification of the instant invention defines "receptor-antagonizing domain" as "a ligand that specifically binds to a receptor "(see page 9), for the purposes of this rejection, an antibody will be defined as "a ligand that specifically binds to a receptor."

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 11/14/2002.

Conclusion

13. No claims are allowed.

Claims 1-4, 6, 9-10, 22,and 24-25 are rejected.

Claims 7-9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
June 16, 2004

GARY NICKOL
PRIMARY EXAMINER